Trend Watch

Polypharmacy of Schizophrenia

by Peter Dussias, MBA; Amir H. Kalali, MD; and Leslie Citrome, MD, MPH

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ABSTRACT

In this article, we investigated the current practice for treatment of schizophrenia. According to our data, physicians consider one-product regimens 53 percent of the time. Two-product regimens are considered 29 percent of the time, and regimens of three or more products are considered 18 percent of the time. At the point of the patient visit, antipsychotic medications comprise 97 percent of treatment regimens. Fifty-six percent of treatment regimens involve only antipsychotic medications. Classes used to supplement antipsychotic medications in the treatment of schizophrenia include antidepressants (20%), mood stabilizers (15%), anti-anxiety (7%) drugs, and drugs to treat extrapyramidal symptoms (6%). An expert commentary is also included with the data.

KEY WORDS

Schizophrenia, antipsychotics, antidepressants, mood stabilizers, extrapyramidal symptoms

INTRODUCTION

To better understand polypharmacy in the management of schizophrenia, we investigated drug classes physicians consider in the selection of treatments to control schizophrenia symptoms.

METHODS

We obtained data on product treatment regimens from SDI's Physician Drug and Diagnosis Audit (PDDA) database from May 2009 to April 2010 for schizophrenic disorders as defined by *International Classification of Diseases, Ninth Revision* (ICD-9) code 295. PDDA captures data on disease states and associated therapies from 3,200 office-based physicians representing 30 specialties across the United States. PDDA provides a non-longitudinal sample of activities that represent the physician intent of office-based physicians. PDDA does not follow the patient subsequent to drug issuance to ensure adherence.

RESULTS

As seen in Figure 1, physicians consider one-product treatment regimens 53 percent of the time. Two-product regimens are considered 29 percent of the time, and regimens of three or more products are considered 18 percent of the time. According to our data in Figure 2, 56 percent of product regimens are for antipsychotics alone. Twenty percent of treatment regimens are for an antipsychotic supplemented by an antidepressant. Other classes reported to supplement antipsychotics in the management of schizophrenia include mood stabilizers (including lithium or antiepileptics, 15%), anti-anxiety drugs (7%), and drugs to treat

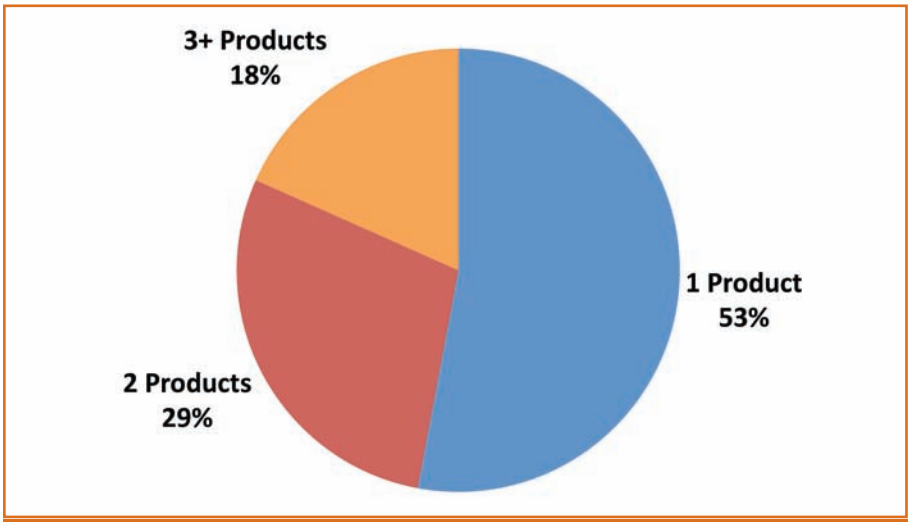

FIGURE 1. Product regimens for schizophrenia
SOURCE: SDI PDDA, Diagonsis 295, May 2009 to April 2010

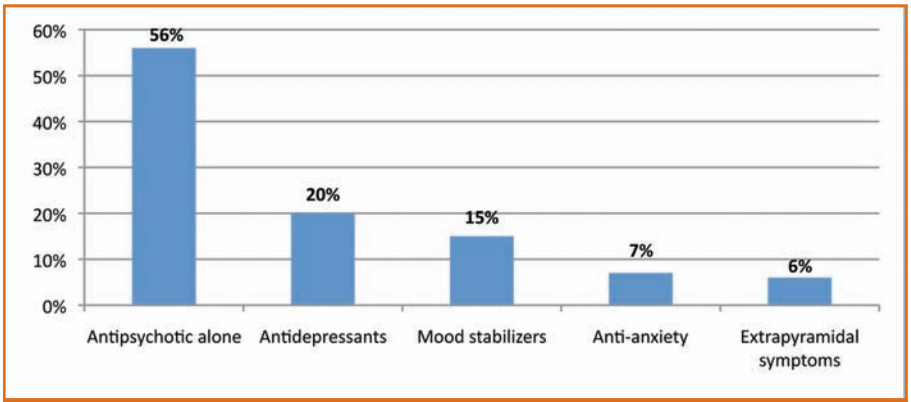

FIGURE 2. Antipsychotic regimens (antipsychotic supplemented by additional class) for treatment of schizophrenia.
SOURCE: SDI PDDA, Diagonsis 295, May, 2009 to April 2010

extrapyramidal symptoms (6%). Overall, antipsychotic medications comprise 97 percent of treatment regimens.

EXPERT COMMENTARY

by Leslie Citrome, MD, MPH

Combination medication strategies for the treatment of schizophrenia are commonly used to treat refractory psychotic symptoms, mood instability, aggressivity, negative symptoms, and cognitive impairment. This acknowledges that schizophrenia is a multidimensional disorder with several treatment targets. Additional medications are often prescribed to relieve adverse effects of the primary medications, such as the use of anticholinergic medications for extrapyramidal symptoms, beta-blockers for akathisia, and a variety of potential anorexic agents for antipsychotic-induced body weight gain. It is no surprise then that many patients end up on a complex regimen that is difficult for the clinician to keep track of and even more difficult for the patient to adhere to.

The results presented here from survey data from office-based physicians in the United States provide somewhat lower rates of coprescribing with other antipsychotics and mood stabilizers than those reported regarding medication utilization within the network of state-operated psychiatric hospitals in New York.[1,2] This may be related to obvious differences in disease severity and/or chronicity between outpatients and inpatients receiving intermediate and long-term care.

Unfortunately, for many of the combination treatments used, the evidence base is lacking. For example, randomized, controlled trials of antipsychotic combinations have not consistently demonstrated a clinically relevant advantage for the combination over monotherapy.[3] Intriguing, however, is the possibility of mitigating some adverse effects of antipsychotics by using combinations.[4]

The use of mood stabilizers, such as lithium or anticonvulsants, added to antipsychotic medication, is also not well supported by the literature. In contrast to the use of combinations of second-generation antipsychotics with mood stabilizers for bipolar disorder, this treatment strategy for schizophrenia has not been approved by regulatory agencies.[5,6] Preliminary data of the usefulness of lithium as an adjunctive agent have been negated by later studies. Similarly, large randomized, controlled trials of adjunctive valproate and adjunctive lamotrigine completed in the wake of early and promising efficacy signals from smaller studies have failed to replicate the initial findings. Also problematic is the lack of well-designed clinical trials of adjunctive mood stabilizers in treatment-refractory schizophrenia or persistent aggressive behavior in schizophrenia, two populations for which there remains a pressing therapeutic need for better treatments. Pragmatically, on an individual patient basis, there may be some advantages to be gained by adding a mood stabilizer to a

medication regimen, but these must be weighed against potential adverse effects, and outcomes closely monitored so that discontinuation of the mood stabilizer is prompt should benefits not accrue.

In the future, we can expect medications specifically approved as adjunctive to antipsychotic therapy. Efforts by the pharmaceutical industry and also by partnerships between industry and academia are underway to develop potential treatments for cognitive dysfunction associated with schizophrenia. More information about the Treatment Units for Research on Neurocognition and Schizophrenia (TURNS) program can be found at http://www.turns.ucla.edu/.

In general, the search for efficacious adjunctive treatments has been a slow process, marked by several failures.[7–11] The most promising therapeutic target appears to be glutamate, the main excitatory neurotransmitter in the brain that is present in most neurons. There are several different types of glutamate receptors with differing effects on glutamatergic function.[12]

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